



# Rabies Surveillance and Prevention

Recommendations for Providers



## Rabies - Background

- Lyssavirus belonging to the Rhabdoviridae family
  - “bullet-shaped virus”
  - RNA virus
- Rabies is a virus that affects the central nervous system in mammals
  - Virus travels within the nerves
  - Within the brain, virus multiplies rapidly
    - Signs of disease begin to develop





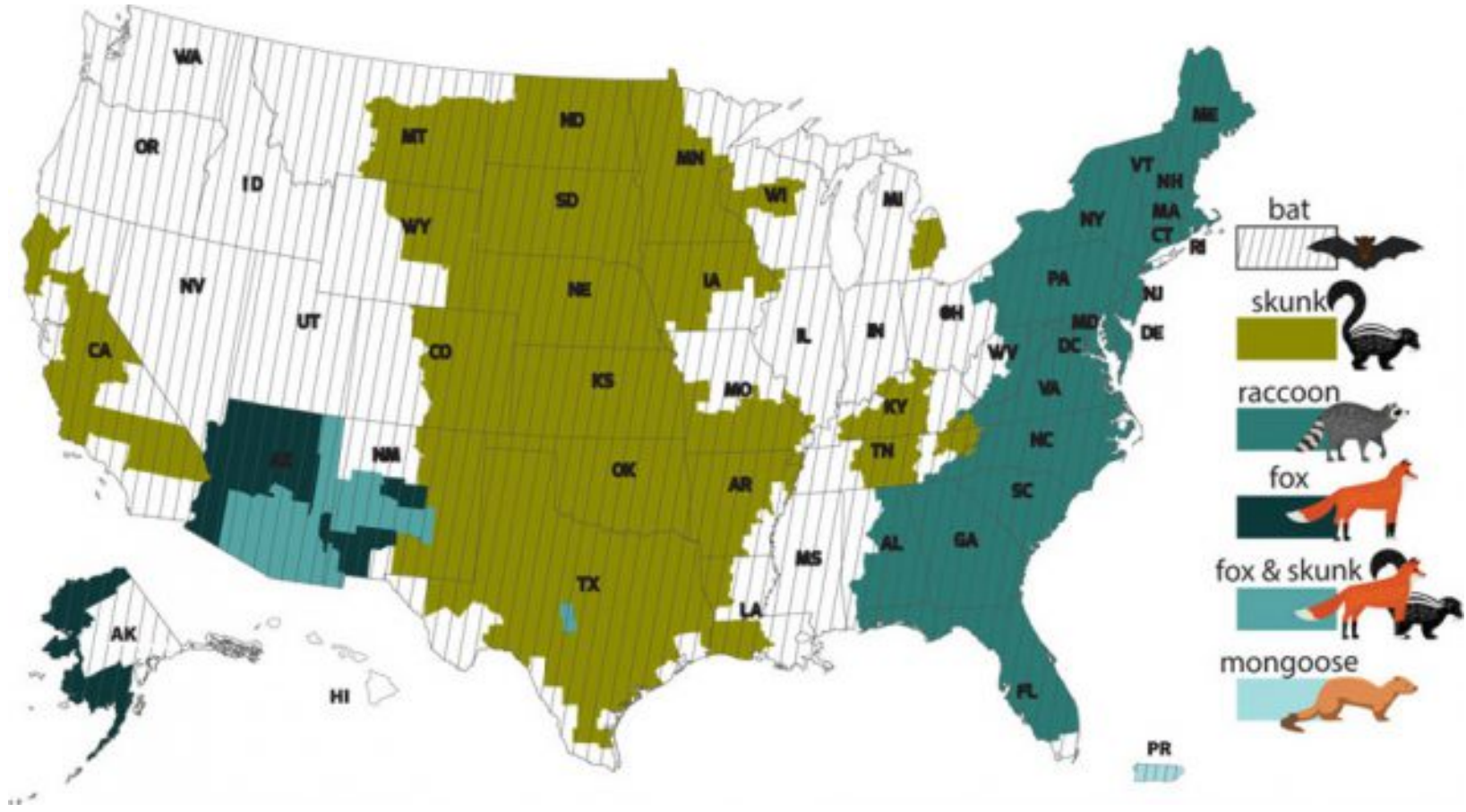
## Rabies - Background

- In the most recent report (2018) more than 90 percent of rabies cases reported each year in the United States occurred in wildlife
  - 33% bats
  - 30.3% raccoons
  - 20.3% skunks
  - 7.2% foxes
- Skunks are responsible for most reported animal cases in North Dakota
- Different variants (bat, skunk, raccoon, etc.)

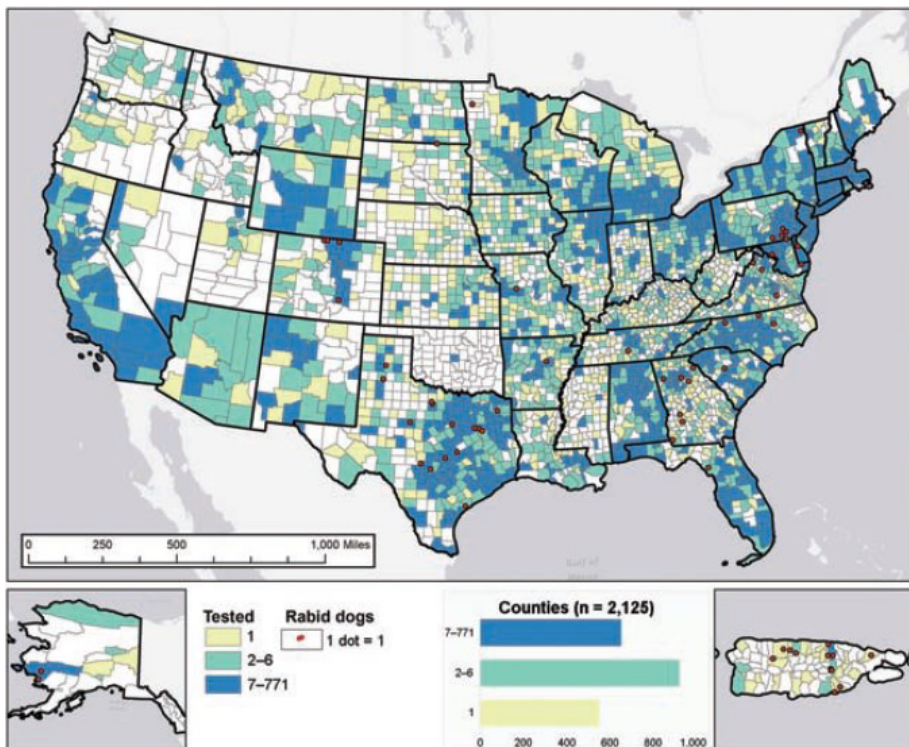
[https://www.cdc.gov/rabies/location/usa/surveillance/wild\\_animals.html](https://www.cdc.gov/rabies/location/usa/surveillance/wild_animals.html)



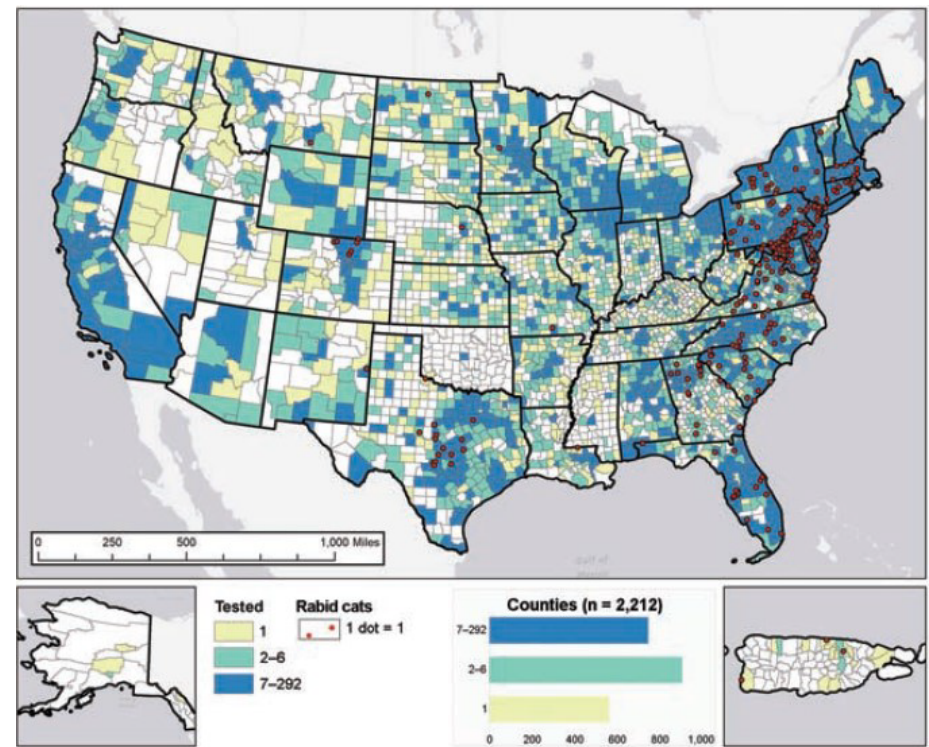
# Terrestrial Rabies Reservoirs(2019)



# Rabid Cats and Dogs Reported in the U.S. (2018)



**Figure 7**—Reported cases of rabies involving dogs, by county, during 2018. Histogram represents number of counties in each category for total number of dogs submitted for rabies testing. Point locations for rabid dogs were randomly selected within each reporting jurisdiction.



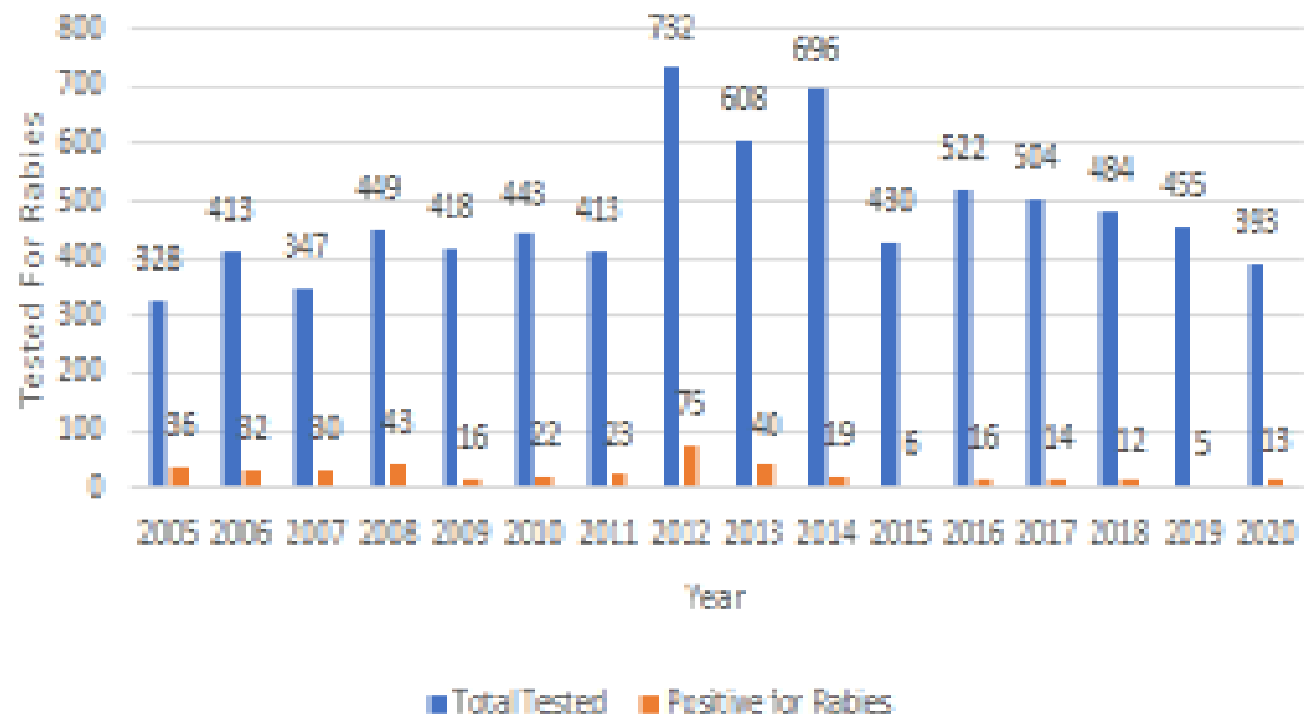
**Figure 8**—Reported cases of rabies involving cats, by county, during 2018. Histogram represents number of counties in each category for total number of cats submitted for rabies testing. Point locations for rabid cats were randomly selected within each reporting jurisdiction.



# Rabies in North Dakota

- Average of 477 animals tested per year
  - 732 animals tested in 2012
- Average of 25 positive rabies animals per year
  - 5% positive

Positive Rabies in ND 2005-2020



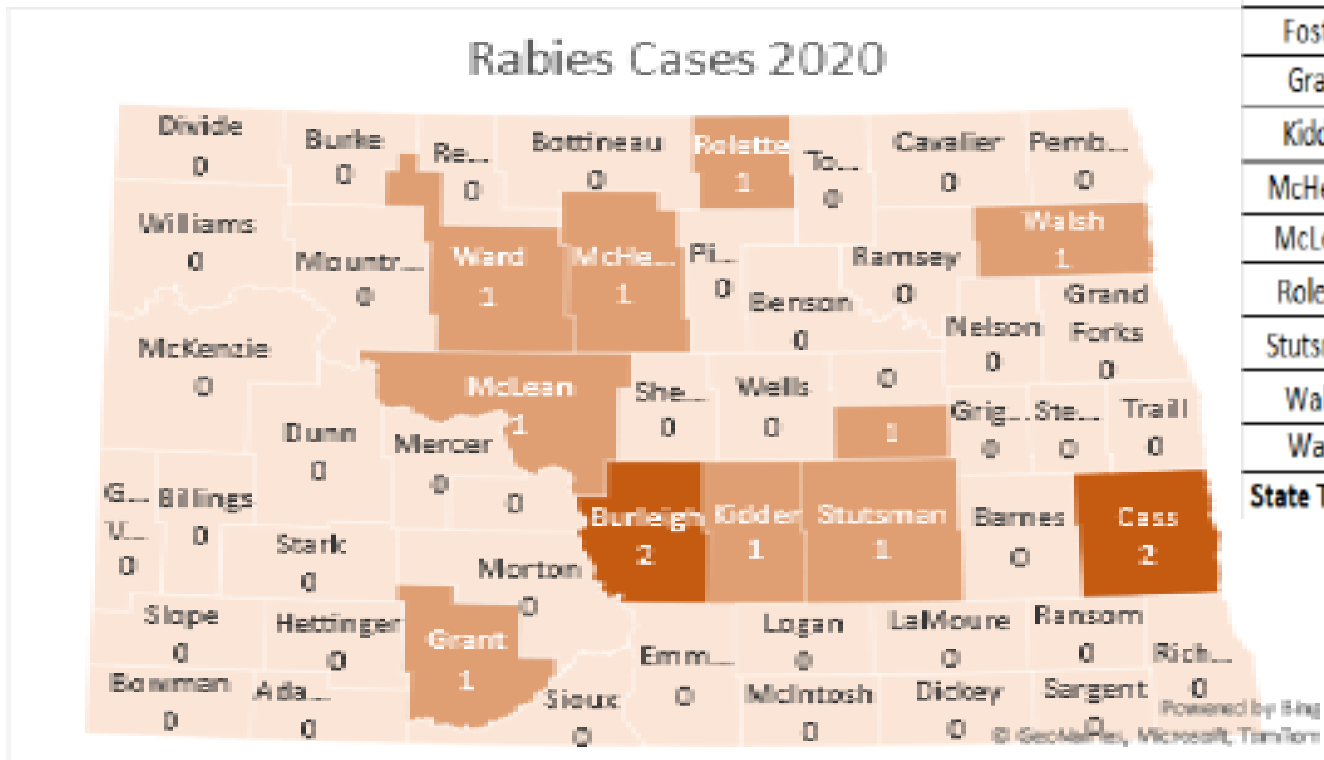




# Rabies in North Dakota

- Positive Animals Rabies Cases by County, North Dakota, 2020

Rabies Positive Animals in ND			
County	Bat	Cow	Skunk
Burleigh			2
Cass	1		1
Foster			1
Grant	1		
Kidder			1
McHenry			1
McLean	1		
Rolette			1
Stutsman			1
Walsh		1	
Ward		1	
<b>State Totals</b>	<b>3</b>	<b>2</b>	<b>8</b>





# Human Rabies Around the World

- Rabies is a global health issue
- Human cases are underreported
  - Most rabies cases occur in countries with inadequate diagnostic facilities and surveillance systems for rabies
- Exposure to rabid dogs is the cause of over 90% of human exposures and over 99% of human rabies deaths<sup>1</sup>
- Limited access to healthcare and resources



1- <http://www.cdc.gov/rabies/location/world/index.html>



# US soldier dies of rabies after dog bite in Afghanistan

Published May 03, 2012 NewsCore

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WASHINGTON – A 24-year-old American soldier died of rabies after being bitten by a dog last year in Afghanistan, US health officials said Thursday following an investigation into the rare case.

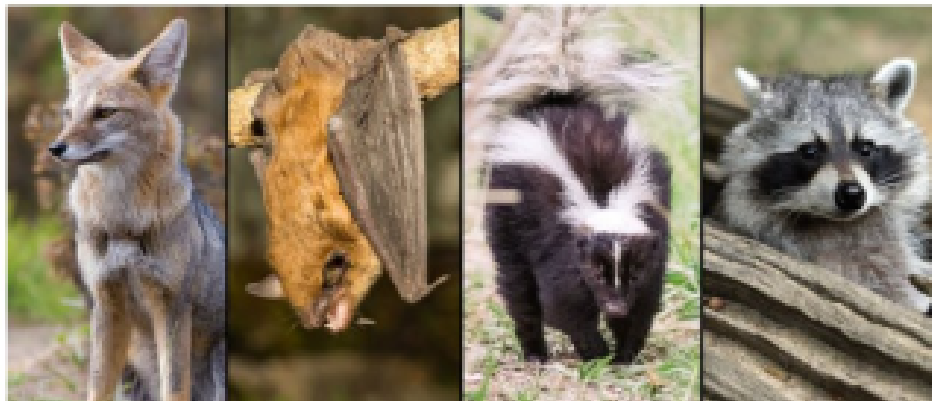
## An Idaho man died of rabies. It was the first death of its kind since 1978.

BY: AUDREY DUTTON - NOVEMBER 17, 2021 7:30 AM



The healthy soldier started experiencing symptoms of shoulder and tingling sensations in his hands soon after arriving at Fort Drum, in August 2011.

At the time he was admitted to an emergency room, he was delirious and hydrophobic, meaning he developed an intense fear of water because of the painful muscle spasms he experienced while



 In the U.S., rabies is mostly found in wild animals including bats, foxes, raccoons and skunks. (Courtesy of the Centers for Disease Control and Prevention)

A man from Boise County died last week from a rabies infection, according to state and local health officials. It is the first such death in Idaho since 1978.



# Rabies in the U.S.

- Human cases – 1 to 3 each year
  - 25 human cases 2009-2018
    - Variant Type
      - Bat(13), Dog(8), Raccoon(3), unknown (1)
    - Exposure Type
      - Bite (8), Contact (8), Transplant (1), unknown (8)
      - Estimated 25,000 to 35,000 human exposures<sup>1</sup>  
Most from domestic animal exposure
- Cases of human and animal rabies are mandatory reportable conditions to the NDDoH
  - Website - [www.ndhealth.gov/disease/Rabies/](http://www.ndhealth.gov/disease/Rabies/)



1- [http://www.cdc.gov/rabies/location/usa/surveillance/human\\_rabies.html](http://www.cdc.gov/rabies/location/usa/surveillance/human_rabies.html)



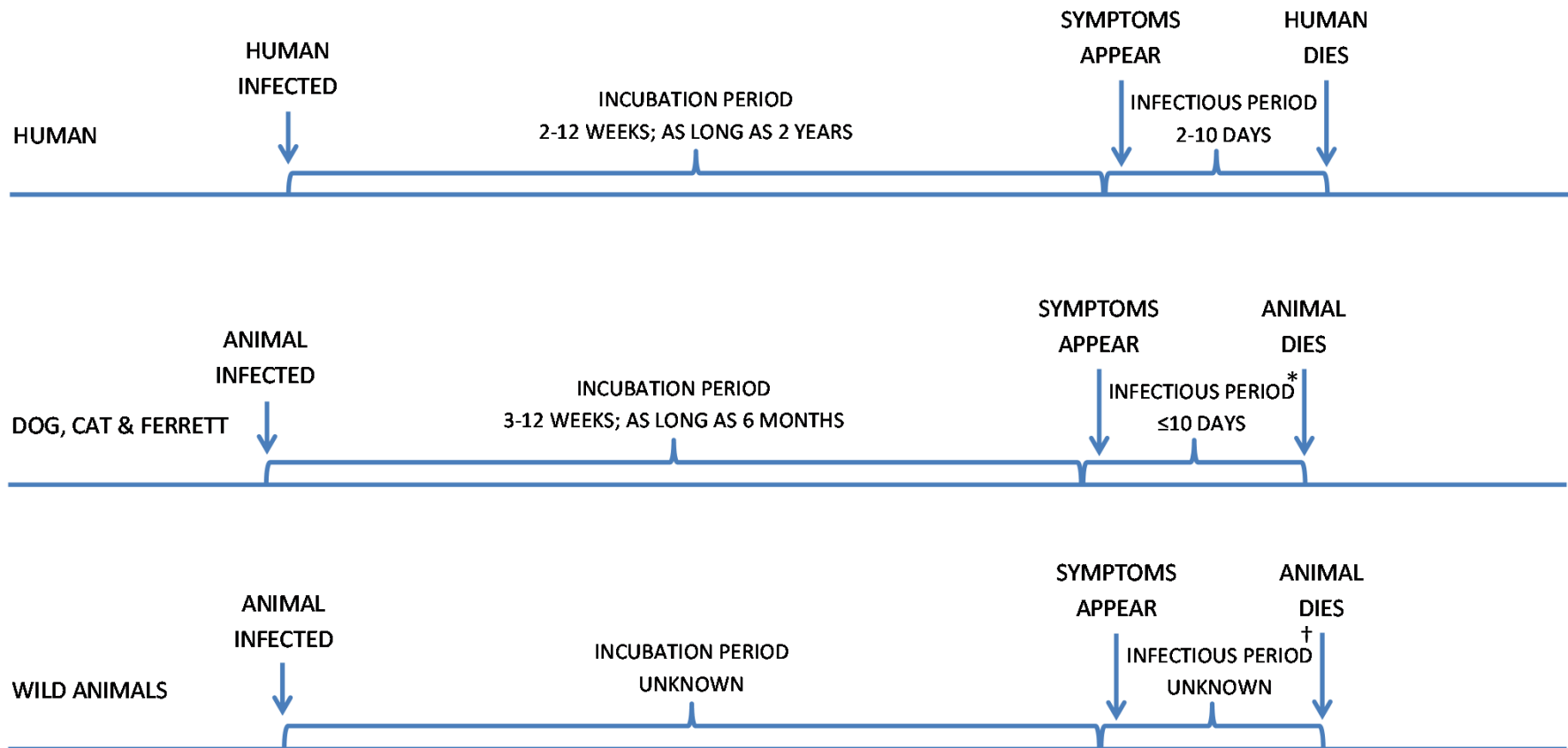
## Cost of PEP

- Cost to fully vaccinate is variable, average of \$2,500<sup>1</sup> to \$5,000
  - Approx. \$506,250 in vaccination costs
  - Est. \$364,000 potentially avoided costs by vaccinating pets, quarantine, etc.





# Rabies Exposure Timeline

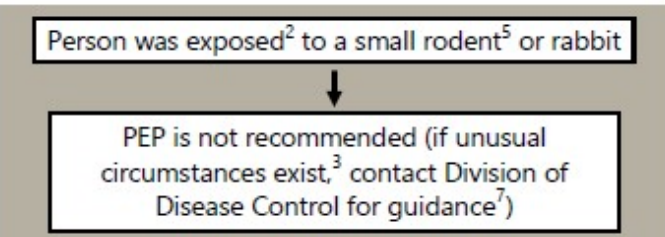
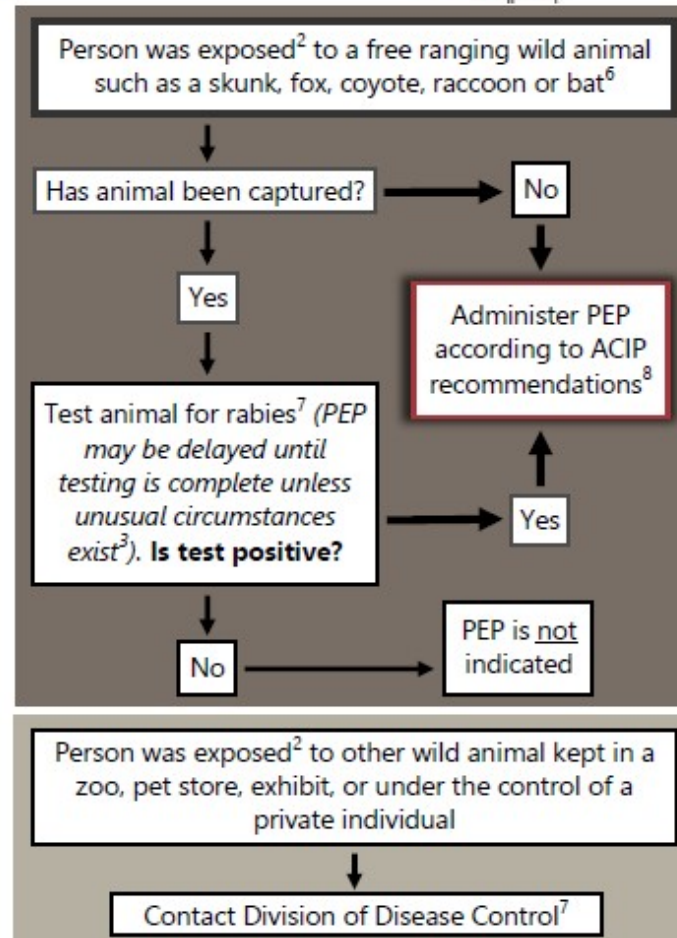
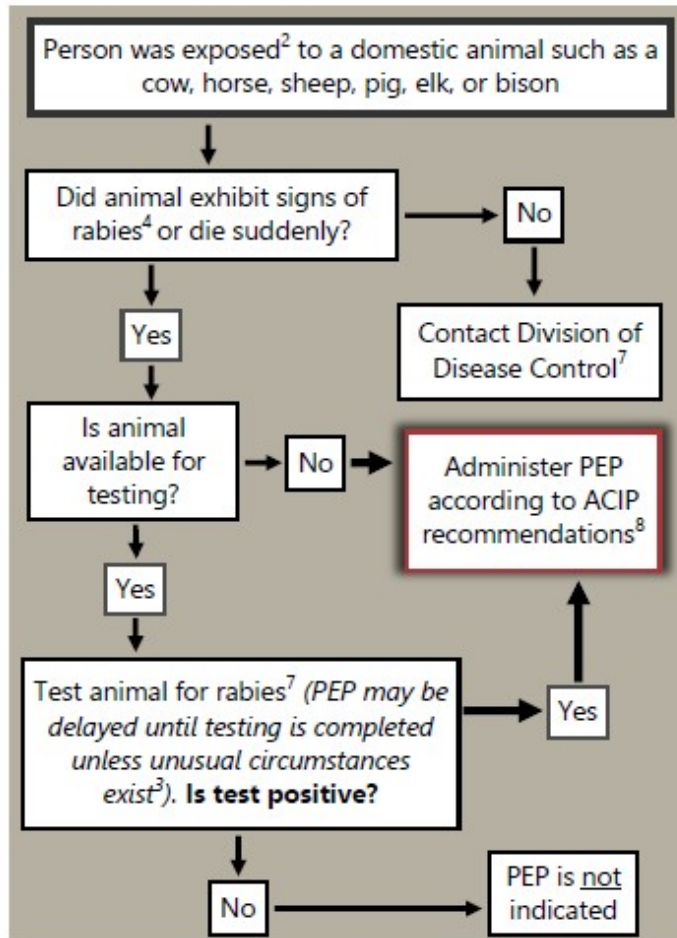
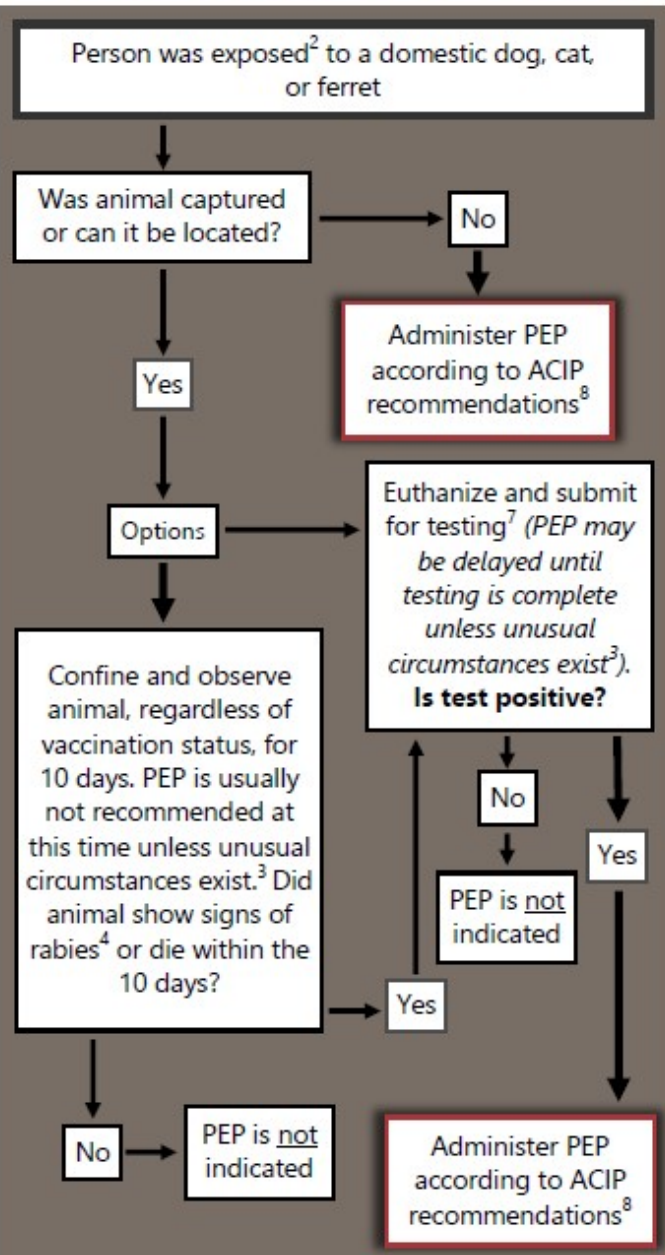


\* May be infectious for a number of days before clinical signs appear. When investigating human exposures, it is recommended to consider the 10 days prior to onset of clinical signs (or date of death if no signs of illness) as part of the animal's infectious period.

† It is unknown as to how long a wild animal can shed rabies virus in its saliva before clinical signs of illness appear. Any exposure to a wild animal that cannot be tested, even if apparently healthy, should be treated as if the animal is rabid.



# Rabies Exposure Assessment<sup>1</sup> Algorithm



1. Risk assessment should include the type of exposure, the species of animal involved, and circumstances of the exposure incident (e.g., appearance and behavior of animal, provoked or unprovoked attack, etc.).
2. Two types of exposures exist. A bite exposure is any penetration of the skin by teeth. A nonbite exposure is contamination of open wounds, abrasions (including scratches) or mucous membranes (e.g., mouth, nose, eyes) with saliva or other potentially infectious material (e.g., cerebrospinal fluid, spinal cord, brain tissue). Direct contact with a bat is also an exposure (see 6). If no exposure occurred, PEP is not necessary.
3. If the animal exhibited any sign(s) of rabies (see 4), the attack was vicious or unprovoked, or the bite(s) occurred in the head or neck region, consider starting PEP immediately.
4. Signs of rabies may include any of the following: excitability, vicious attacks, biting, agitation, restlessness, aggression, lack of fear, excessive salivation, aversion to water, inability to swallow or drink, muscular dysfunction, coordination or gait irregularities, paralysis, convulsions, avoidance of contact with humans or other animals, lethargy, and loss of appetite.
5. Small rodents include squirrels, hamsters, mice, rats, gerbils, chipmunks, gophers, moles, and voles.
6. Any potential exposure to a bat requires a thorough evaluation. See reverse for additional information.
7. See reverse for contact information for rabies exposure consultation and rabies testing laboratories in ND.
8. See reverse for ACIP recommendations for rabies PEP.



## Bat Exposures

Any direct contact between a human and a bat should be evaluated for an exposure. If the person is reasonably certain a bite, scratch, or mucous membrane exposure did not occur, PEP is not necessary. If the bat is available for testing and the test is negative, PEP is not necessary. The following situations may qualify as exposures requiring consideration of PEP:

- Finding a bat with a person who may be unaware that direct contact had occurred (ex. An adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person)
- A deeply sleeping person awakens to find a bat in the room

***Please contact the Division of Disease Control for consultation regarding potential exposure to bats.***

## ND Contact Information

### Rabies Exposure Consultation in ND

**NDDoH Division of Disease Control**  
800-472-2180 or 701-328-2378  
*After hours contact 701-220-0819*

### Rabies Testing Laboratories in ND

**NDDoH Division of Microbiology**  
701-328-6272  
*After hours contact 701-400-2772 or State Radio at 800-472-2121*

**NDSU Veterinary Diagnostic Laboratory**  
701-231-7527 or 701-231-8307

### Animal Health and Wildlife Contacts in ND

**North Dakota Department of Agriculture, State Veterinarian's Office**  
701-328-2655

**North Dakota Game and Fish Department**  
701-328-6300

## Post-exposure Prophylaxis (PEP) for Rabies

The Advisory Committee on Immunization Practices (ACIP) recommends that unless a person has previously completed the rabies vaccination regimen (either pre- or post-exposure) or is immunosuppressed, PEP should always consist of human rabies immune globulin (HRIG or RIG) and four vaccine doses. RIG and the first dose of the 4-dose vaccine should be administered as soon as possible after exposure (day 0). Additional doses of vaccine should be administered on days 3, 7, and 14. Previously vaccinated persons should receive 2 vaccine doses, the first dose as soon as possible after the exposure (day 0) and the second dose 3 days later (day 3). Persons with immunosuppression should receive RIG and five vaccine doses. RIG and the first dose of the 5-dose vaccine should be administered as soon as possible after exposure (day 0). Additional doses of vaccine should be administered on days 3, 7, 14, and 28.

Every attempt should be made to adhere to the ACIP's recommended vaccination schedules. For most minor deviations from the schedule (i.e., delays of a few days for individual doses), vaccination can be resumed as though the patient was on schedule. If substantial deviations from the schedule occur, reinitiation of the entire series may be required. Contact the Division of Disease Control for guidance on deviations from the vaccine schedule.

**For additional information on rabies PEP and vaccine availability in North Dakota, please visit [www.ndhealth.gov/disease/Rabies/Vaccine](http://www.ndhealth.gov/disease/Rabies/Vaccine).**

### References

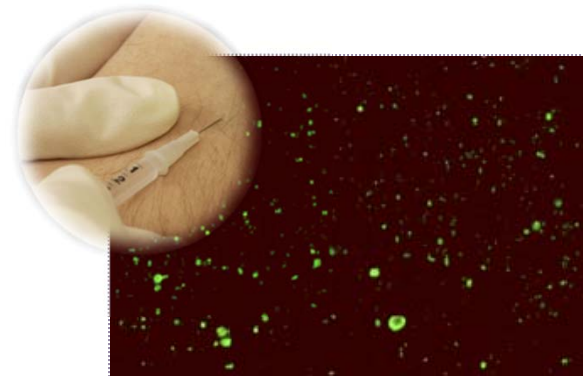
1. Human Rabies Prevention – United States, 2008: Recommendations of the Advisory Committee on Immunization Practices (ACIP). CDC MMWR 2008; 57 (No. RR-3).
2. Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices (ACIP). CDC MMWR 2010; 59 (No. RR-2).
3. Compendium of Animal Rabies Prevention and Control, 2016: National Association of State Public Health Veterinarians, Inc. Journal of the American Veterinary Association. Vol.248, No.5, March 1, 2016.





# Rabies Exposure

- Definition of rabies exposure
  - Introduction of virus-laden saliva into the body through a bite or contact of the virus-laden saliva or neural tissue with an open wound or the mucous membranes.
    - *Blood, feces, urine is not infectious*
- All animal bites or other possible exposures should be assessed by a healthcare provider!






# Rabies Case Management

- Determine if exposure or possible exposure (bite or non-bite)
  - Bite from a rabid animal that breaks skin
  - Saliva from a rabid animal that comes into contact with:
    - Open sore, cut or wound in the skin
    - Mucus membrane of mouth, eyes or nose
    - Brain tissue/fluid contact with opening in skin
  - Scratches not exposures – except cats

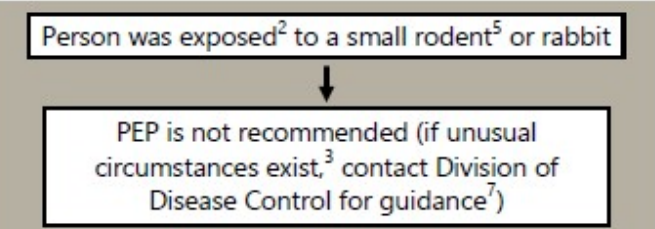
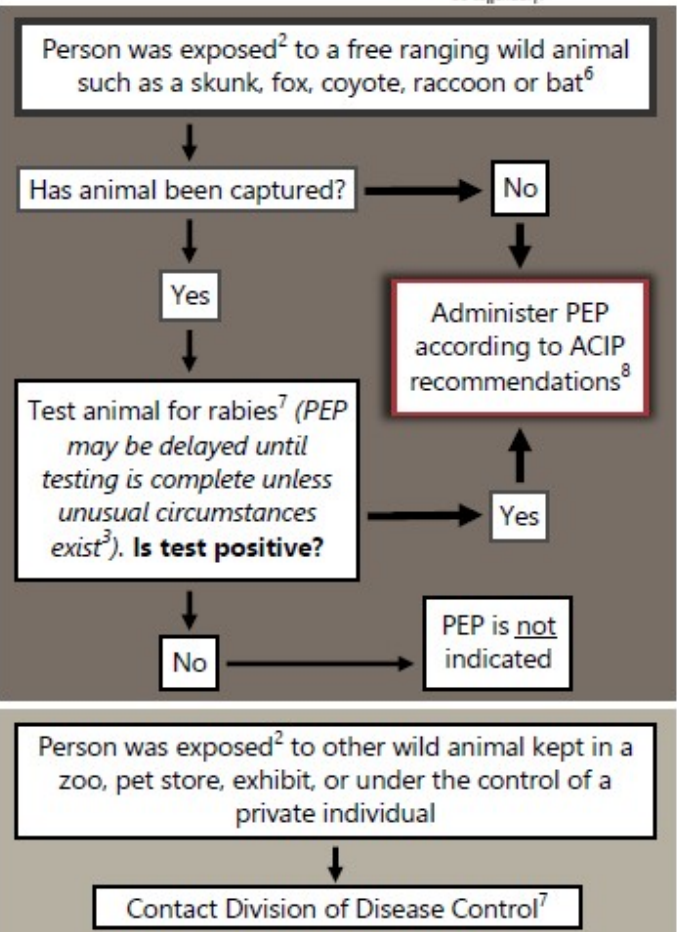
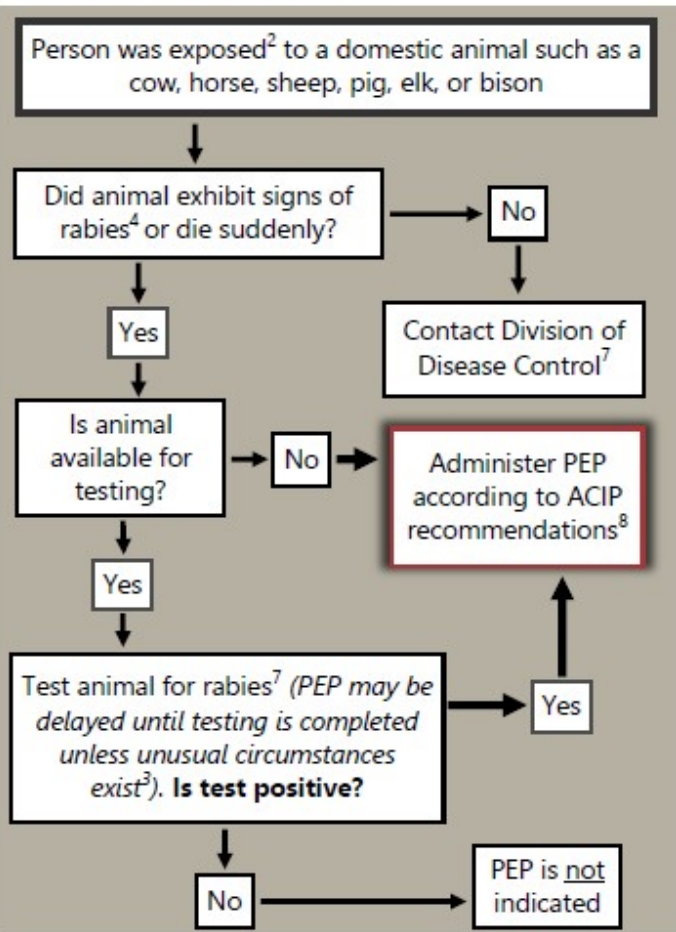
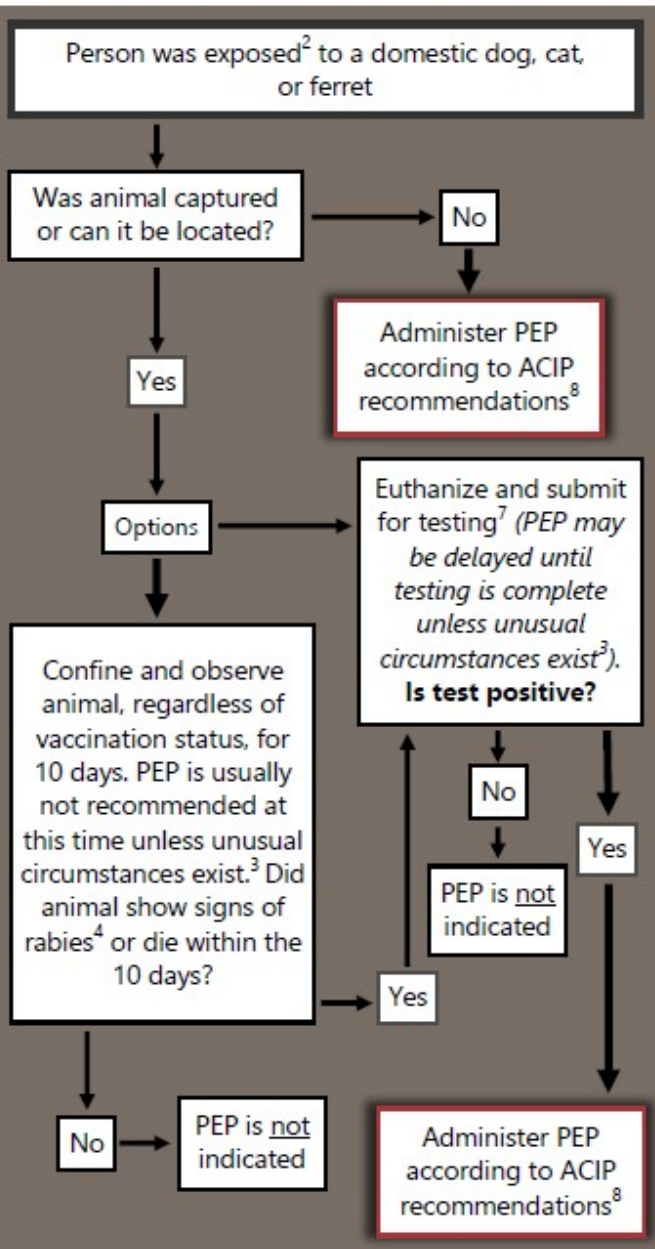


## Rabies Case Management, cont.



- Access the exposure (high risk, wound cleansing, exposure site, etc.)
    - Domestic or wild animal
    - Vaccination status, current
    - Provoked or unprovoked attack
    - Health status/behavior of animal
    - Animal available or reasonably attainable for testing or quarantine
  - Bites to the head or neck may want to consider starting rabies PEP before test results or quarantine period is over
- 

# Rabies Exposure Assessment<sup>1</sup> Algorithm



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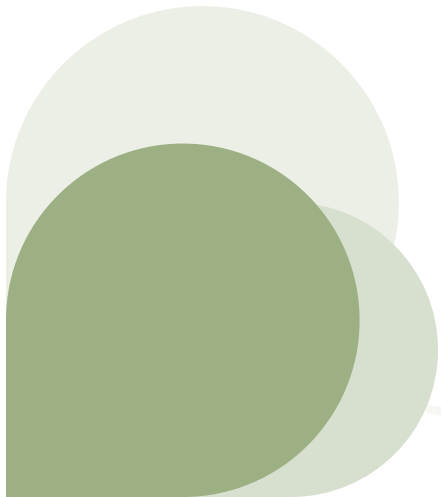
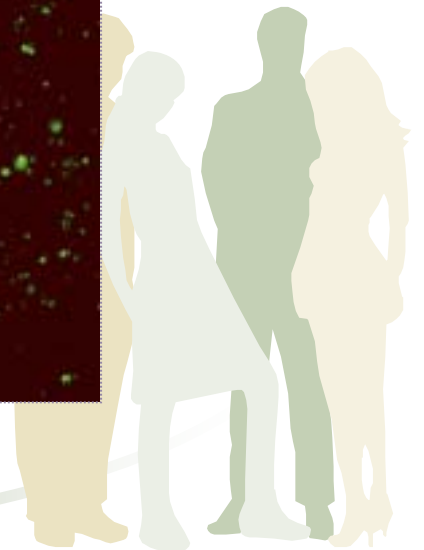
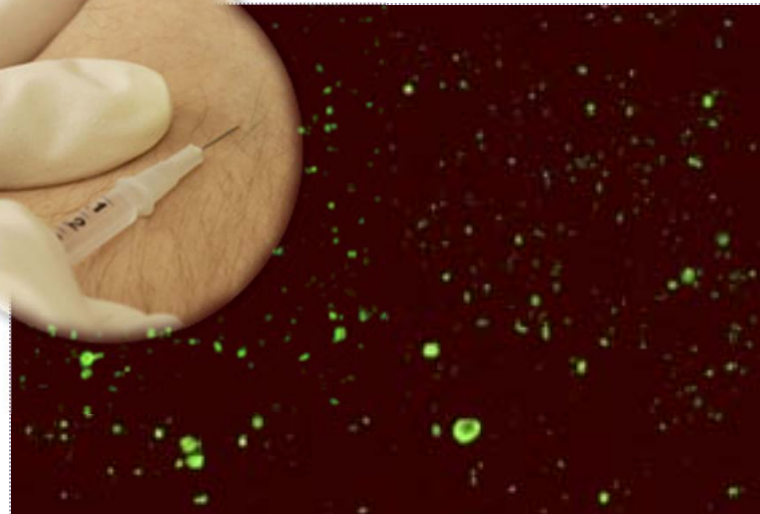


# Rabies In Domestic Animals

- Signs and symptoms of rabies develop when the rabies virus reaches and multiplies in the brain of the animal
- Signs and symptoms (changes in behavior or health)
  - Viciousness
  - Biting
  - Restlessness
  - Loss of appetite
  - Nervousness
  - Lack of fear
  - Excessive salivation
  - Sluggishness
- Incubation variable, typically 3 to 8 weeks (range 10 days to 6 months)
- Infectious period up to 5 days before symptoms appear
  - Dogs, cats and ferrets only (unknown in all other animals)



# Human Rabies Vaccine







# ACIP Rabies Workgroup

- Used evidence-based process for reduced vaccination schedule
- Reviewed six areas:
  - Rabies virus pathogenesis
  - Experimental animal models
  - Human immunogenicity studies
  - Prophylaxis effectiveness in humans
  - Documented failures of prophylaxis
  - Vaccine safety



# Rabies Virus Pathogenesis

- The key to preventing rabies is to neutralize the virus before it enters the central nervous system
- Local virus neutralization
  - Immediate and thorough wound cleansing
  - Passive immunization (RIG)
- Active immunization – vaccine series

**Appropriate PEP Ensures Patient Survival**



# Experimental Animal Models

- No statistically significant differences in survivorship were observed among animal groups receiving different number of doses of vaccine
- No differences were detected in immunogenicity and efficacy of PEP with 2, 3, or 4 dose schedules



# Human Clinical Studies

- All healthy patients developed rabies virus neutralizing antibody by day 14



Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies:  
Recommendations of the Advisory Committee on Immunization Practices. MMWR Mar. 19, 2010;59[No. RR-2]



# Prophylaxis Effectiveness

- Of people who have died from rabies
  - Did not receive PEP
  - Receive some PEP
    - Without RIG
    - Delays in initiation
  - Substantial PEP deviations from recommended schedule
- No case who received timely wound care, RIG and 4 doses of vaccine



# Documented PEP Failures

- 21 fatal human cases (some form of PEP)
  - 20 cases developed illness and most died before day 28
    - Virus infection of the nervous system occurred before the date of 5<sup>th</sup> dose
- None from failure to receive 5<sup>th</sup> dose





# Vaccine Safety/Economics

- No adverse events from failure to receive 5<sup>th</sup> dose
- Fewer adverse reactions
- Presumed cost savings of reduced schedule
  - Travel expenses
  - Time away from work
  - Health-care worker time



## Reduced 4 Dose Schedule

- Evidence reviewed and presented to ACIP during June 2009 meeting
  - Accepted the recommended 4 dose schedule for PEP for previously unvaccinated persons
    - Exception immunosuppressed individuals – 5 dose recommendation remains unchanged
- CDC released provisional recommendations few months later
- Recommendations for use published in **MMWR** on **March 19, 2010**



# MMWR™

**Morbidity and Mortality Weekly Report**

[www.cdc.gov/mmwr](http://www.cdc.gov/mmwr)

Recommendations and Reports

March 19, 2010 / Vol. 59 / No. RR-2

## **Use of a Reduced (4-Dose) Vaccine Schedule for Postexposure Prophylaxis to Prevent Human Rabies**

**Recommendations of the Advisory Committee  
on Immunization Practices**





# Vaccination Schedule

- Post-exposure prophylaxis – MMWR pg. 6

**TABLE 3. Rabies postexposure prophylaxis (PEP) schedule — United States, 2010**

Vaccination status	Intervention	Regimen*
Not previously vaccinated	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (e.g., povidine-iodine solution) should be used to irrigate the wounds.
	Human rabies immune globulin (HRIG)	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around and into the wound(s), and any remaining volume should be administered at an anatomical site (intramuscular [IM]) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area <sup>†</sup> ), 1 each on days 0, <sup>§</sup> 3, 7 and 14. <sup>¶</sup>
Previously vaccinated**	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area <sup>†</sup> ), 1 each on days 0 <sup>§</sup> and 3.

\* These regimens are applicable for persons in all age groups, including children.

<sup>†</sup> The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.

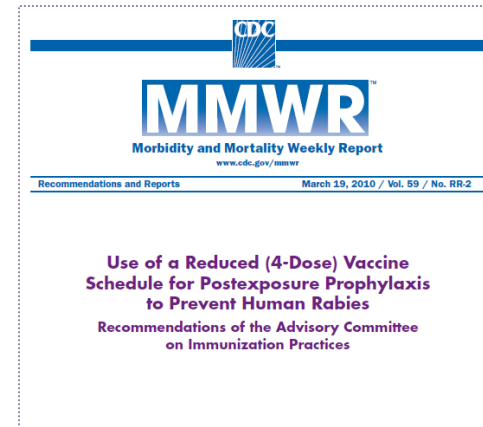
<sup>§</sup> Day 0 is the day dose 1 of vaccine is administered.

<sup>¶</sup> For persons with immunosuppression, rabies PEP should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.

\*\* Any person with a history of pre-exposure vaccination with HDCV, PCECV, or rabies vaccine adsorbed (RVA); prior PEP with HDCV, PCECV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

# Treatment of Wounds & Vaccination

- Not-previously vaccinated
  - Wound cleansing
    - Soap & Water, wound irrigation.
  - Rabies immune globulin (RIG)
    - 20 IU/kg body weight
    - If possible, full dose should be infiltrated around the wound site.
      - Remainder in anatomical site distant from vaccination site.
  - Vaccine \*
    - 1 mL, IM (deltoid area, or outer thigh for small children).
    - 4-doses: Days 0, 3, 7 & 14.
    - Immunosuppression: 5 doses on days 0, 3, 7, 14 and 28





# Treatment of Wounds & Vaccination

- Previously vaccinated
  - Wound cleansing
    - Soap & Water, wound irrigation.
  - Rabies immune globulin (RIG)
    - Should NOT be administered!
  - Vaccine
    - 1 mL, IM (deltoid area, or outer thigh for small children).
    - 2-doses: Days 0 & 3.



# Rabies Vaccination

- Pre-exposure vaccination
  - 2-doses of 1 mL, IM (deltoid area, or outer thigh for small children).
    - Days 0,7
  - NO RIG
- Booster doses
  - 1-1mL, IM booster dose if does not have evidence of virus neutralizing antibodies in serum at 1:5 serum dilution by the RFFIT (rapid fluorescent focus inhibition test).



# Rabies Vaccine Review

- **Pre-exposure**
  - 2 doses
    - Days 0, 7
- **Post-exposure** (previously vaccinated)
  - 2 doses
    - Days 0 and 3
- **Post-exposure** (previously unvaccinated)
  - 4 doses\*
    - Days 0, 3, 7 and 14
  - RIG administer
- Immunosuppression – PEP 5 doses on days 0, 3, 7, 14 and 28





# Rabies in Humans

- The first symptoms of rabies may be very similar to those of the flu including general weakness or discomfort, fever, or headache. These symptoms may last for days.
- There may be also discomfort or a prickling or itching sensation at the site of bite, progressing within days to symptoms of cerebral dysfunction, anxiety, confusion, agitation. As the disease progresses, the person may experience delirium, abnormal behavior, hallucinations, and insomnia.



Photo credit: CDC



# Antemortem Rabies Testing

- State health departments should be the primary contact for physicians during consultation about possible human rabies cases. After consultation with physicians, it may be deemed necessary to send human samples for rabies testing to the Rabies Laboratory at the Centers for Disease Control and Prevention (CDC).
- All four samples are required to rule out rabies:
  - Nuchal biopsy
  - Saliva
  - Serum
  - CSF



# Rabies in Humans

- There is no single effective treatment for rabies once clinical signs are evident. The following resources provide current research and thoughts regarding treatment options. These are not intended to serve as recommendations for rabies treatment.
  - Management of Rabies in Humans (CID)
    - <http://cid.oxfordjournals.org/content/36/1/60.full.pdf+html>
  - Milwaukee Rabies protocol
    - <http://www.chw.org/display/PPF/DocID/33223/router.asp>



## Resources

- Disease Control – 800.472.2180 or 701.328.2378
- CDC MMWR Human Rabies Prevention --  
<http://www.cdc.gov/mmwr/PDF/rr/rr5703.pdf>
- CDC MMWR Reduced 4-Dose Schedule --  
<http://www.cdc.gov/mmwr/pdf/rr/rr5902.pdf>
- CDC Rabies website --  
<http://www.cdc.gov/rabies/>
- NDDoH Rabies website --  
<http://www.ndhealth.gov/disease/Rabies/>